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BAPEN Symposium 4: All in one and one for all: off the shelf parenteral nutrition; Cordon Bleu or greasy spoon?

Nutritional requirements of surgical and critically-ill patients: do we really know what they need?

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Malnutrition remains a problem in surgical and critically-ill patients. In surgical patients the incidence of malnutrition ranges from 9 to 44%. Despite this variability there is a consensus that malnutrition worsens during hospital stay. In the intensive care unit (ICU), 43% of the patients are malnourished. Although poor nutrition during hospitalisation may be attributable to many factors, not least inadequacies in hospital catering services, there must also be the question of whether those patients who receive nutritional support are being fed appropriately. Indirect calorimetry is the 'gold standard' for determining an individual's energy requirements, but limited time and financial resources preclude the use of this method in everyday clinical practice. Studies in surgical and ICU patient populations have been reviewed to determine the 'optimal' energy and protein requirements of these patients. There are only a small number of studies that have attempted to measure energy requirements in the various surgical patient groups. Uncomplicated surgery has been associated with energy requirements of 1.0–1.15 × BMR whilst complicated surgery requires 1.25–1.4 × BMR in order to meet the patient's needs. Identifying the optimal requirements of ICU patients is far more difficult because of the heterogeneous nature of this population. In general, 5.6 kJ (25 kcal)/kg per d is an acceptable and achievable target intake, but patients with sepsis or trauma may require almost twice as much energy during the acute phase of their illness. The implications of failing to meet and exceeding the requirements of critically-ill patients are also reviewed.

Nutritional requirements: Energy expenditure: Critical illness

Malnutrition in surgical and critically-ill patients

Malnutrition remains a problem in surgical and critically-ill patients. McWhirter & Pennington (1994) have found, using a combination of anthropometric measures and weight-loss history, that 27% of general surgical patients are undernourished on admission. Of these patients 63% are considered to be moderately or severely malnourished. In another study (Giner *et al.* 1996) 44% of surgical patients have been reported to be malnourished according to serum albumin and weight:height ratios. More recent evidence, however, suggests that the incidence of malnutrition in

surgical patients may be falling. Fettes *et al.* (2002) have reported that only 9% of patients admitted for gastrointestinal surgery are malnourished. Despite differences between these studies in the incidence of malnutrition, all three observed that nutritional status worsens during hospital admission. Up to 34% of patients (Fettes *et al.* 2002) experience clinically significant weight loss (>5%) post-operatively.

In the intensive care unit (ICU) 43% of the patients are reportedly malnourished (Giner *et al.* 1996), although nutritional assessment of these patients is notoriously difficult (Manning & Shenkin, 1995) and this percentage may be an

Abbreviation: ICU, intensive care unit.

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underestimate of the true extent of the problem. Giner *et al.* (1996) have found that malnourished critically-ill patients have significantly more complications ($P < 0.001$) and are less likely to be discharged from hospital ($P < 0.05$) than their well-nourished counterparts. Not surprisingly, in the sickest subgroups of patients malnutrition contributes less to outcome.

Although poor nutrition during hospitalisation may be attributable to many factors, not least inadequacies in hospital catering services, there must also be the question of whether those patients who receive nutritional support are being fed appropriately.

Predictive equations for estimating energy requirements

Indirect calorimetry is considered by many researchers to be the gold standard for determining energy expenditure in individuals over relatively short periods of time. If measurement conditions are standardised and the operator is familiar with the technique then useful and accurate measurements can be obtained in many clinical settings. However, limited access to indirect calorimeters, along with time constraints associated with clinical practice, restrict its use. Instead, clinicians rely on equations, of which there are >200, to help predict a patient's energy expenditure. Few of these equations have been designed for acutely-ill or chronically-ill patients. For example, the Harris-Benedict equation (Harris & Benedict, 1919) was developed from indirect calorimetry measurements made in normal-weight healthy adults in the early 1900s. Stress factors or correction factors need to be added so that equations that have been derived from healthy subjects can be used to predict energy expenditure in sick or injured patients. In contrast, the Ireton-Jones equation (Ireton *et al.* 1986) was developed from indirect calorimetry measurements, albeit short periods of measurement, in hospitalised patients. Two equations were developed (one for spontaneously breathing patients and one for ventilator-dependent patients), and subsequent studies have shown that the Ireton-Jones equation correlates well with measured energy expenditure (Gagliardi *et al.* 1995; Wall *et al.* 1995), probably because it takes into account factors that affect energy expenditure (e.g. diagnosis, presence of obesity and ventilator status).

The use of stress factors may introduce substantial error into estimations of energy expenditure, since there is no definitive guide as to the stress factors that should be used in different clinical situations. For example, the Elia (1990) normogram (Fig. 1) suggests a 20–50% stress factor for patients with sepsis requiring mechanical ventilatory support. The value the clinician ultimately decides to use can be very subjective and dependent on their experience in dealing with different patient types. Many investigators have performed indirect calorimetry studies, in supposedly specific patient groups, in an attempt to quantify more precisely their energy expenditure and therefore their energy requirements. Long *et al.* (1979) have reported that in sepsis energy expenditure is $1.8 \times$ estimated BMR. Frankenfield *et al.* (1994) have reported a similar observation, with patients with sepsis expending $1.9 \times$ BMR.

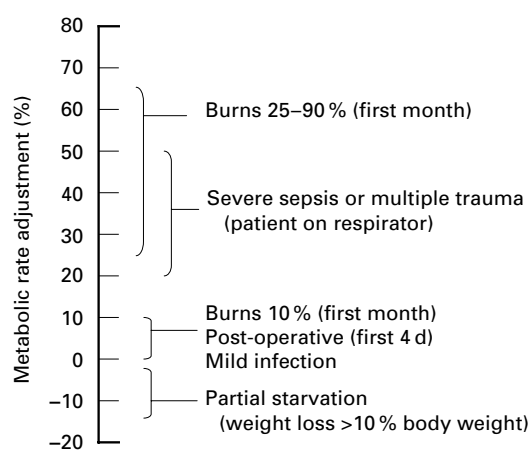


Fig. 1. Normogram for predicting stress factors associated with injury and illness. (Adapted from Elia, 1990.)

The same investigators, however, failed to show agreement for the energy expenditure associated with skeletal trauma. The variability between these studies and many others that have attempted to measure the energy expenditure associated with different disease states or clinical conditions is related to the fact that often the study population is poorly defined, such that comparisons between studies cannot easily be made. Although there is some agreement between Long *et al.* (1979) and Frankenfield *et al.* (1994) in relation to energy expenditure in patients with sepsis, their study populations were very different. Long *et al.* (1979) defined sepsis simply as the presence of pyrexia whilst Frankenfield *et al.* (1994) looked at post-trauma patients requiring mechanical ventilation who developed multiple organ dysfunction secondary to sepsis. Clearly, this latter population was the sickest and yet the study results do not reflect this fact, probably because the patients were not breathing spontaneously and many of them were sedated; both these interventions are known to reduce energy expenditure. When adopting stress factors from the literature it is essential to demonstrate that the reference population and the patient population for whom they are to be used are the same or similar. Many factors can influence an individual's energy expenditure (Table 1).

No studies to date have made allowances for energy deficits that occur as a result of abnormal losses. These losses, which include wound, nasogastric and fistula outputs and haemofiltrate, in the vast majority of patients, where

Table 1. Factors commonly associated with either an increase or decrease in energy expenditure in hospitalised patients

Factors increasing energy expenditure	Factors reducing energy expenditure
Pyrexia	Sedation
Disease state	Anaesthesia
Renal replacement therapy (e.g. haemofiltration)	Neuromuscular blocking agents
Surgery	Hypothermia
Abnormal losses	Starvation
Infection	Reduced mobility
Pain	

Table 2. Energy content of abnormal losses associated with wound, nasogastric and fistula outputs and haemofiltrate (Values are medians and ranges)

	Total volume (ml/24 h)			Energy value of freeze-dried material (g)						Energy value of original substance (ml)						Total energy loss (24 h)					
	Median	Range	kcal	Median	Range	kcal	Median	Range	kcal	Median	Range	kcal	Median	Range	kcal	Median	Range	kcal	Median	Range	kcal
Nasogastric aspirate (4 d)	175	50–250	0.98	0.82–1.15	4.13	3.46–4.83	0.004	0.03–0.06	0.17	0.14–0.26	6.2	1.9–15.2	26	8–64							
Haemofiltrate (3 d)	34 700	33 500–34 700	0.21	0.18–0.22	0.9	0.77–0.93	0.00014	0.00014–0.00017	0.006	0.006–0.007	49.8	47.9–57.9	209	201–243							
Fistula output (6 d)	625	400–1000	0.94	0.7–1.15	3.95	2.95–4.83	0.04	0.03–0.05	0.157	0.132–0.230	22.6	15.7–225.8	95	66–230							
Fistula output (4 d)	750	700–1925	0.96	0.83–1.1	4.04	3.47–4.59	0.05	0.03–0.07	0.201	0.117–0.273	43.3	30.7–53.3	182	129–224							
Wound drainage (5 d)	700	700–800	1.15	1.04–1.17	4.84	4.36–4.91	0.05	0.05–0.09	0.210	0.198–0.393	37.6	33.1–65.5	158	139–275							

volumes are low, probably make little contribution to energy losses. However, it has been shown that wound and intestinal effluents contain between 0.04 and 0.05 kJ (0.15 and 0.21 kcal)/ml (Table 2) and in patients with high-output fistulas or wounds, energy losses can amount to 15% of their average daily energy expenditure (Reid *et al.* 1999). For this reason, and other reasons listed in Table 1, clinical judgement is still important if stress factors are to be adopted appropriately and fine-tuned to meet an individual's actual requirements.

Post-operative energy expenditure

There is a surprising lack of studies measuring energy expenditure in post-operative patients, especially in patients following gastrointestinal surgery for whom the greatest problems in achieving and maintaining adequate nutritional support would be expected. Long *et al.* (1979) have suggested that a 24% stress factor is used for patients following elective abdominal surgery but, as a result of improved surgical techniques in the last 20 years, more recent studies have suggested stress factors of this magnitude are more appropriate for patients following complicated surgery (Barak *et al.* 2001). For patients who had undergone abdominal surgery, Kemper & Beredjikian (1992) have reported energy expenditures between 5.5 and 6.0 kJ (23 and 25 kcal)/kg per d, whilst Barak *et al.* (2001), in a more complicated group, have measured energy expenditures in the range 5.5–7.4 kJ (23–31 kcal)/kg per d. On the basis of this limited data it may be safe to assume that following abdominal surgery most or all of the patient's energy needs would be met by providing 6.0–7.0 kJ (25–30 kcal)/kg per d. The incidence of malnutrition in surgical patients and, perhaps more importantly, the fact that their nutritional status worsens during hospital admission (McWhirter & Pennington, 1994; Giner *et al.* 1996; Fettes *et al.* 2002) suggests that it is not the absolute amount of energy these patients receive that is important but whether they are fed at all. Fasting patients for prolonged periods both pre- and post-operatively is still common practice and undoubtedly contributes more to their worsening malnutrition than whether they are fed 6.0 or 7.0 kJ (25 or 30 kcal)/kg per d.

Neurosurgical patients are worthy of a special mention, since marked increases in energy expenditure have been reported in this patient group. Energy expenditure values reported in patients following subarachnoid haemorrhage (Kasuya *et al.* 1998), for example, exceed those traditionally associated with extensive burn injury. Grade I or II subarachnoid haemorrhage has been found to be associated with a 36 (SD 27) % increase in energy expenditure (e.g. $1.36 \times \text{BMR}$) whilst more severe subarachnoid haemorrhage (\geq grade III) is associated with a 71 (SD 58) % increase in energy expenditure. Similarly, acute severe head injury, even in the presence of sedation and neuromuscular blockade, is accompanied by energy expenditure values that are 130–135% above the predicted BMR (Weekes & Elia, 1996; Bruder *et al.* 1998). Further increases are associated with the cessation of sedation and neuromuscular blockade (Bruder *et al.* 1998; McCall *et al.* 2003). The increases in metabolic rate observed in

neurosurgical patients are only evident for the first 3 weeks following the initial injury (Weekes & Elia, 1996); however, because the increases in metabolism are so great, nutritional status worsens considerably during this time.

Energy expenditure in critical illness

General intensive care unit population

There is enormous variability in the increases in energy expenditure associated with critical illness. This variability is largely a result of the heterogeneous nature of this population, especially in non-specialist units to which patients are admitted from a variety of clinical specialties. Carlsson *et al.* (1984) have measured energy expenditure in an ICU population consisting of patients with trauma or sepsis and medical patients, all mechanically-ventilated. Energy expenditures were reported to range from 70 to 126% of the predicted BMR or were on average 6.9 (SD 0.3) kJ (28.8 (SD 1.2) kcal)/kg per d. Swinamer *et al.* (1987), also in a general ICU population, have reported energy expenditures 47.3 (SD 22.3) % above the predicted value. Both Green *et al.* (1995) and Reid & Campbell (2001) have measured energy expenditure continuously in mechanically-ventilated patients with multiple organ dysfunction. Green *et al.* (1995) found that patients expend on average 8.1 kJ (34 kcal)/kg per d, although the range for individuals is 6.1–13.7 kJ (25.6– 57.6 kcal)/kg per d or 89–184% of predicted BMR. Reid & Campbell (2001) reported markedly lower energy expenditure values (median 6.2, range 4.8–9.1 kJ (median 26, range 20.3–38.3 kcal)/kg per d), but the patients in this study were less sick, with a mortality rate of only 35% compared with 60% in the study by Green *et al.* (1995).

Trauma and sepsis

Even when investigators focus on more-specific patient groups within the ICU there is still some variability in measured energy expenditure. Trauma has been associated with energy expenditures of 96 (Carlsson *et al.* 1984), 120 (Brandi *et al.* 1999) and 155 (Frankenfield *et al.* 1994) % of the predicted BMR. These values equate to (kJ/kg per d) 7.3 (SD 0.3), 6.4 (SD 1.0) and 8.6 (SD 1.4) (kcal/kg per d; 30.5 (SD 1.2), 27 (SD 4) and 36 (SD 6)) respectively. These differences are predominantly a result of differences in the severity of injury between study populations. Uehara *et al.* (1999) have reported much higher energy expenditure in trauma patients (14 kJ (59 kcal)/kg per d, equivalent to 982 (SD 123) kJ (4123 (SD 518) kcal)/d), but on examination ten of the twelve patients studied had a head trauma as their primary injury and therefore data are not comparable with the previously mentioned studies in which patients with head injuries were excluded. Three studies of severe sepsis spanning 11 years have reported very similar energy expenditure data (Shizgal & Martin, 1988; Frankenfield *et al.* 1994; Uehara *et al.* 1999). Shizgal & Martin (1988) reported an average energy expenditure of 11.1 (range 3.4–20.7) kJ (46.8 (range 14.4–87.0) kcal)/kg per d compared with 10.5 (SD 1.9) kJ (44 (SD 8) kcal)/kg per d (Frankenfield *et al.* 1994) and 11.2 kJ (47 kcal)/kg per d

(Uehara *et al.* 1999) in the later studies. Energy intakes of this magnitude correlate with energy expenditures of approximately 786 kJ (3300 kcal)/d (Frankenfield *et al.* 1994; Uehara *et al.* 1999).

Importance of clinical judgement

In the present review the interchangeable use of the terms energy expenditure and energy requirements (practised by so many researchers) has been avoided, since it is important to emphasise that these two terms do not have the same meaning. Energy expenditure can be measured or predicted, but energy requirement relates to an individual and takes into account much more than just a value derived from indirect calorimetry or from an equation; it must be based on clinical judgement. For example, a clinician may increase an individual's energy requirements to allow for repletion or anabolism, similarly energy may be reduced for weight loss, hypercapnia or glycaemic control. In the ICU appropriate feeding often involves more clinical judgement than adherence to predicted or measured energy expenditure data. Clinicians should avoid the dictum 'more is better' and should instead heed the rule 'minimize harm'. Critically-ill patients undergo dramatic depletion of lean body mass (especially skeletal muscle; Fig. 2), and this process appears to occur irrespective of the adequacy of nutritional support (Streat *et al.* 1987; Green *et al.* 1995; Monk *et al.* 1996; Hart *et al.* 2002; Reid *et al.* 2004). It is essential that the clinician has realistic expectations of what nutritional support can accomplish, especially in the sickest patients. It is unlikely that a positive N balance, meaningful weight gain and increased visceral proteins can be achieved by meeting or exceeding a critically-ill patient's energy expenditure. However, overambitious nutritional support may precipitate metabolic complications and organ dysfunction. High energy intakes have been associated with increased ventilator dependence and length of stay in the ICU (Hart *et al.* 2002), whereas hypoenergetic feeding (60% energy

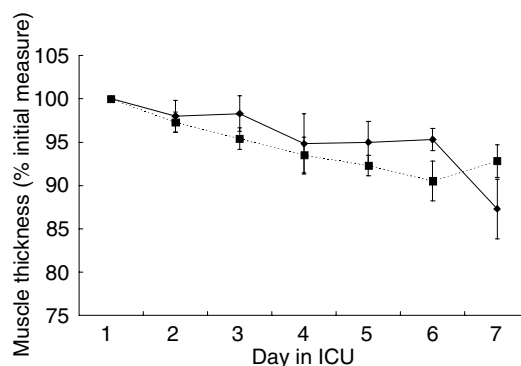


Fig. 2. Skeletal muscle wasting in critically-ill patients according to energy balance. Muscle thickness was measured using ultrasound (Reid *et al.* 2004). Values are mean and standard deviations represented by vertical bars. The mean daily rate of muscle wasting for patients in positive energy balance (◆) and for those in negative energy balance (■) was -1.1% ($P > 0.05$). ICU, intensive care unit.

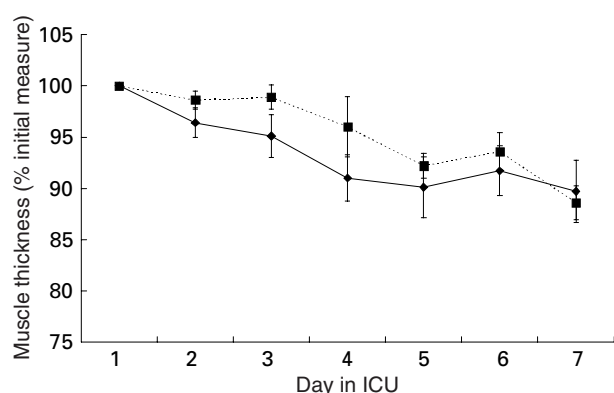


Fig. 3. Skeletal muscle wasting in critically-ill patients according to nitrogen balance. Muscle thickness was measured using ultrasound (Reid *et al.* 2004). Values are mean and standard deviations represented by vertical bars. Mean daily rate of muscle wasting in patients in positive nitrogen balance (◆) was -1.6% compared with -1.3% in patients in negative nitrogen balance (■). The difference was not statistically significant ($P > 0.05$).

expenditure) has been associated with reduced ventilator dependence, length of stay in the ICU and antibiotic therapy (Dickerson *et al.* 1986). Although not advocating this approach in all critically-ill patients, it is worthy of consideration in patients with chronic respiratory compromise who are particularly difficult to wean from artificial ventilatory support.

Recommended protein requirements in surgical and critically-ill patients

There has been much less research done on protein requirements, which has made the task of determining optimum protein requirements more difficult. Protein dynamics in surgical stress are influenced, like energy expenditure, by both the severity of illness and the underlying nutritional status. With mild injury such as elective surgery, there is a normal or slightly depressed rate of protein synthesis, but with severe injury or critical illness the rates of both protein synthesis and breakdown are increased (Tashiro *et al.* 1991). A negative protein balance develops in the latter group because the increase in breakdown exceeds the increase in protein synthesis. This is a teleological response to mobilise amino acids from skeletal muscle to the plasma for utilisation by the liver and other tissues. In the short term this response is beneficial, but if it is prolonged the continued erosion of lean skeletal muscle may severely compromise a patient's rehabilitation and recovery.

Protein requirements in the range of $1.25\text{--}2.0\text{ g/kg per d}$ have been recommended by several investigators (Elia, 1990; American Society of Parenteral and Enteral Nutrition, 2002). Excessive protein intakes, like excessive energy intakes, are unlikely to correct the negative protein balance associated with critical illness and, even if they were to do so, they would not prevent the erosion of skeletal muscle (Fig. 3). Ishibashi *et al.* (1998) have measured protein balance in a critically-ill population, each of whom was randomised to receive protein intakes

of 0.9 , 1.2 or 1.5 g/kg per d . Although the patients in all three groups were reported to be in negative protein balance, protein intake of 1.2 g/kg per d was found to be associated with a 50% improvement in the protein balance; intakes $>1.2\text{ g/kg per d}$ conferred no further benefit.

Conclusion

Despite the vast amount of nutrition research that has been conducted over the last 25 years, there are surprisingly few studies that have been able to demonstrate clinically-relevant benefits with nutritional support, especially in relation to critical illness. The present review has demonstrated that even the appropriate quantity of energy and/or protein does not appear to consistently improve patient outcomes, especially in relation to body composition (Streat *et al.* 1987; Green *et al.* 1995; Monk *et al.* 1996; Reid *et al.* 2003), but in excess can unfavourably influence outcome (Hart *et al.* 2002). As a result of these findings attention has shifted from the quantity of nutritional support to the quality of the nutrients it contains. In particular, nutrients with demonstrated immune-modulating properties (immunonutrients, glutamine, arginine, *n-3* fatty acids, nucleotides and antioxidants) have generated much interest, although a full discussion on this area of nutritional support is beyond the scope of the present review. Benefits have been demonstrated in some patient populations and with certain nutrient combinations, but the findings are inconsistent. There is recent data to suggest that when used inappropriately these immuno-nutrients may also unfavourably influence outcome (Heyland *et al.* 1999). Much research remains to be done in this area.

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